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# (54) Mouldable starch compositions

(57) A particulate, free-flowing starch based formulation comprises

(i) chemically unmodified starch or a mixture of chemically unmodified starch and no greater than 50%, by weight of the chemically unmodified starch, of another hydrophilic material, said starch or mixture being present in an amount of at least 72% by weight, based on the weight of the formulation;

(ii) a texturing agent in an amount of from 0.02% to 1.0% by weight, based on the weight of the formulation;

(iii) one, or a combination of both, of the following components: a lubricant/release agent and a melt-flow accelerator, the one component or the combination of both components being present in an amount of from 0.4% to 5.0% by weight, based on the weight of the formulation; and

(iv) water in an amount of at least 10%, based on the weight of the formulation.

The compositions are used for preparing moulded bodies, e.g. capsules, for filling with pharmaceuticals and other chemicals.

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SPECIFICATION

**A starch based formulation**

This invention relates to a starch based formulation which is particulate and free-flowing and which is useful in manufacturing shaped articles by pressure forming techniques.

It is known to process starch under applied pressure and to manufacture pressure-formed moulded bodies therefrom, for example by means of injection moulding. Preferably, such moulded bodies are manufactured to be filled with pharmaceuticals, comestibles, chemicals and other materials, but, particularly as pharmaceutical capsules for the dosed administration of medicaments. Such capsules consist, as a rule, of a body part and a cap part, which telescopically engage to provide a tightly sealed container.

The manufacture of such pressure-formed capsules from natural starch is described in European Patent Application No. 84 360 940.8 (Publication. No. 118 240).

In industrial fabrication it is necessary to manufacture pressure-formed articles, in particular very thin-walled pharmaceutical capsule parts, with the greatest precision and at high speed. In addition, during manufacture, a minimum number of defective parts should arise in order to minimize subsequent controls and interruptions in the capsule filling operation machine.

Mastering these processing problems has proved to be surprisingly difficult. With the manufacture of very thin-walled parts, for example with wall thicknesses of less than 0.5 mm, the problems intensify.

In particular a very good flow behaviour of the composition to be moulded is necessary, both with reference to the starting powder (freely flowing starch starting mixture), as well as during the injection-moulding process up to the moment at which the moulding composition reaches the fluid state. The molten mass should, to avoid high pressures, flow as easily as possible and should, with regard to the temperature, and the intermixing with additives and water, show as homogenous a distribution as possible.

Furthermore, the injection-moulded parts should be easily removed from the mould, as well as having good dimensional stability, in order to avoid adherence to the wall in the tool or deformation on ejection.

It has, surprisingly, been found that the problems can be solved, if the following requirements are satisfied:

1. a starch starting mixture which is particulate and free-flowing at room temperature is used, which results, under the processing conditions employed, in a moulded article with a practically amorphous wall structure;
2. the viscosity of the molten mass at 90 - 240°C, particularly 140 - 190°C lies between 2500 and 50 Pa s (= Pascal x second), preferably between 2000 and 50 Pa s, and more preferably between 1500 - 50 Pa s; and
3. the glass transition point of the mixture heated in a closed space up to 140 - 190°C should be at least 25°C, preferable at least 45°C and most preferably about 65°C.

According to the present invention there is provided a particulate, free-flowing starch based formulation comprising

(i) chemically unmodified starch or a mixture of chemically unmodified starch and no greater than 50%, by weight of the chemically unmodified starch, of another hydrophilic material, said starch or mixture being present in an amount of at least 72% by weight, based on the weight of the formulation;

(ii) a texturing agent in an amount of from 0.02% to 1.0% by weight, based on the weight of the formulation;

(iii) one, or a combination of both, of the following components: a lubricant/release agent and a melt-flow accelerator, the one component or the combination of both components being present in an amount of from 0.4% to 5.0% by weight, based on the weight of the formulation; and

(iv) water in an amount of at least 10%, based on the weight of the formulation. This formulation enables the requirements specified above to be satisfied.

The formulation specified above permits injection-moulding machines to be driven in continuous 24-hour operation, with minimal errors and without the disadvantages mentioned above.

It has been found that these formulations are suitable for use in processing under applied pressure, for example pressure-moulding, injection-moulding, blow-moulding, extrusion etc.

The basic formulation can include further components, as is described further below.

The chemically unmodified starch employed in this invention may be a vegetable carbohydrate, which mainly consists of amylose and amylopectin. This vegetable starch may be obtained, for example, from potatoes, rice, tapioca, corn, rye, oats, wheat and other plants. Alternatively, or in addition, the chemically unmodified starch may be a starch which has a physically modified structure, such as gelatinized or pre-cooked starch and highly water-soluble starch. Such a starch or a mixture of such starches can be processed in the specified formulation under pressure and raised temperature to form compact moulded bodies.

Preferably the proportion of physically altered starch to natural starch is not higher than 50%, preferably not higher than 20%. Most preferred is natural starch.

The starch is present in the basic somposition in a quantity no less than about 72% by weight based on the weight of the formulation, preferably no greater than 89% to 58%, more preferably in the range of from 75% to 85% by weight based on the weight of the formulation and most preferably between 79% to 83% by weight based on the weight of the formulation.

The starch preferably has an amylose content of from 0 - 70% and amylopectin of 100 - 30%. Most preferred is potato starch.

Suitable as the lubricant/release agent are animal and vegetable fats, individually or in a mixture, in particular such fats which are hydrated and, preferably those which are solid at room temperature. Preferably they have a melting point of over 50°C. These fats are, as a rule, triglycerides with a proportion of $C_{14}$-, $C_{16}$- and $C_{18}$-acids, for example $C_{18}$ (around 65%), $C_{16}$ (around 30%), $C_{14}$ (around 5%).

The quantity of lubricant/release agent employed is preferably 0 - 5% more preferably 0 - 3% and most preferably 0.8 - 1.2% by weight based on the weight of the formulation.

These lubricant/release agents act simultaneously as softening agents, and viscosity depressants so that the addition of such special agents is unnecessary.

The melt-flow accelerator is preferably a mono-or a diglyceride, more preferably a long-chained acid preferably of $C_{14}$-, $C_{16}$-, $C_{18}$- fatty acids and phosphatides, in particular lecithin. The melt-flow accelerator is preferably employed in an amount of from 0 - 5%, preferably 0.1 - 2%, more preferably 0.2 - 1% by weight based on the weight of the formulation.

The sum of the amounts of the lubricant/releasing agent and the melt-flow accelerator should amount to at least 0.4%, and preferably from 1 - 2.2% by weight based on the weight of the formulation.

The texturing agent is preferably titanium dioxide or silicondioxide or a mixture of these compounds. It has been found that such compounds guarantee a free fowing of the starting material as a powder at room temperature and further prevent the formation of bridges in the funnel and at the screw during processing, which hinder the feed of the starting material onto the screw. Through the addition of the texturing agent, the dosing takes place constantly and evenly, and equally fast from cycle to cycle.

It is thus not necessary to granulate or otherwise pretreat the starting material.

The quantity of the texturing agent should be 0.02 - 1% by weight based on the weight of the formulation. For titanium dioxide, the optimum addition quantity lies at about 0.25%, and for silicon dioxide, around 0.1% by weight based on the weight of the formulation. Naturally more titanium oxide or silicon oxide can also be added, though the excess then acts simply as a filler and may negatively influence the properties of the product.

The water is present in a quantity of 10 - 22%, preferably 10 - 20%, more preferably 15 - 19% by weight based on the weight of the formulation. For thin-walled articles the preferred ranges are applicable.

The process conditions depend principally on the starch used; the other components of the formulation and the additives mentioned further below, which may be included if necessary.

The higher the water content, the lower the temperatures and pressures which can be chosen in the injection-moulding process. The lower the water content, the higher the pressures and temperatures to be chosen. The selection of suitable pressures and temperatures is simple and can be carried out easily by the expert. The pressures lie, for thicker-walled articles, in the range of from $300 \times 10^5 N/m^2$ to $3000 \times 10^5 N/m^2$ and, for thinner-walled articles, in the range $600 = 10^5 N/m^2$ to $3000 \times 10^5 N/m^2$, preferably at about $900 \times 10^5 - 1500 \times 10^5 N/m^2$. For extrusion; pressures of a few bars may be used, for example less than 10 bars, depending on the water content. The working temperatures lie predominantly in the range of from 80 - 240°C, preferably 130 - 210°C and most preferably at 150 - 190°C.

Devices known per se, for example injection moulding machines known per se, can be used.

With formulations having the same water content, potato starch can be processed more easily, i.e. with lower pressure and temperature conditions, than wheat starch. The degree of difficulty increases in the order potato starch, wheat starch, corn starch, rice starch. Preferred is potato starch and wheat starch, in particular potato starch.

In the above-mentioned starch formulations, up to 50% of the starch can be replaced by one or more of the other hydrophilic materials for example, gelatin, vegetable proteins such as: sunflower protein, soybean proteins, cotton seed proteins, peanut proteins, rape seed proteins, blood proteins, egg proteins, acrylated proteins; water-soluble polysaccharides such as: alginates, carrageenans, guar gum, agar-agar, gum arabic and related gums (gum ghatti, gum karaya, gum tragacanth), pectin; water-soluble derivatives of cellulose: alkylcelluloses hydroxyalkylcelluloses and hydroxyalkylalkylcelluloses, such as: methylcellulose, hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxyethylmethylcellulose, hydroxpropylmethylcellulose, hydroxybutylmethylcellulose, celluloseesters and hydroxyalkylcelluloseesters such as: celluloseacetylphthalate (CAP), hydroxypropylmethylcellulosephthalate (HPCMP); carboxyalkylcelluloses, carboxyalkylalkylcelluloses, carboxyalkylcelluloseesters such as: carboxymethylcellulose and their alkli metal salts; water-soluble synthetic polymers such as: polyacrylic acids and polyacrylic acid esters, polymethacrylic acids and polymethacrylic acid esters, polyvinylacetates, polyvinylalcohols, poly vinylacetatephthalates (PVAP), polyvinylpyrrolidone, polycrotonic acids; suitable are also phthalated gelatin, gelatin succinate, crosslinked gelatin, shellac, water soluble chemical derivatives of starch, cationically modified acrylates and methacrylates possessing, for example, a tertiary or quaternary amino group, such as the diethylaminoethyl group, which may be quaternized if desired; and other similar polymers.

Preferably the starch is replaced by not more than 3 - 10% of one of these hydrophilic materials.

To the above-mentioned basic formulations can be added a softening agent in a quantity of, preferably, 0.5 - 10% by weight based on the weight of the formulation. In addition, the starting materials may be mixed with liquid additives until they are completely absorbed and firm pourable mixture arises. An excess or a sticking

together of the individual mix grains must be avoided. Such softening agents are, for example, polyalkylene oxides, such as polyethyleneglycols, polypropyleneglycols, polyethylenepropyleneglycols; low-molecular organic softening agents like glycerine, glycerin mono-, di- and triacetate; propyleneglycol, sorbitol, sodium diethyl sulfosuccinate, triethylcitrate, tributylcitrate.

The sum of the weight parts of water and softening agent should preferably not exceed the specified maximum contents for water. Preferably, therefore, the sum of water and softening agents amounts to 10 - 22%, preferably 10 - 20%, most preferably 15 - 19% by weight based on the weight of the formulation.

The mixture can also be dyed. Suitable dyestuffs are, for example, known azo dyes or organic or inorganic pigments, or naturally occurring dyestuffs. Preferred are inorganic pigments, such as iron or titanium oxides in amounts of from 0.001 - 10%, preferably 0.5 - 5%, by weight based on the weight of the formulation.

As mentioned above, the formulation of the present invention can be used in all types of molding techniques under applied pressures such as pressure-molding, injection-molding, blow-molding or extrusion and it is possible to produce such articles as containers, bottles, sheets, sacks, films, packaging materials, tubes, rods, pharmaceutical capsules etc, in all the numerous variations known.

The present invention will now be illustrated by reference to the following Examples:

*Example 1*

A composition consisting of 81 parts of natural potato starch, one part of hydrated triglyceride containing the fatty acids $C_{18}$:$C_{16}$:$C_{14}$ in a ratio of 65:31:4 weight percent, 0.7 parts lecithin, 0.3 parts titanium dioxide and 17 parts water is mixed in a powder mixer for 10 minutes. Thereafter a freely flowing powder is obtained. This powder is filled into the funnel of an injection-moulding machine and, at a temperature of 180°C and a pressure of 1500 bar, injected into an injection moulding tool for capsule main and sealing parts whose mould wall temperature lies at 40°C. After cooling and ejecting from the mould a dimensionally stable capsule main or sealing part is obtained, which can easily be processed on a filling machine.

With this mixture the injection moulding machine can easily be driven in 24-hour operation without interruptions to the machine or detectable defects to the capsule parts being produced.

Analogous results were obtained using different compositions, the details of which are set forth in Table 1:

| No. | Starch Type | % | Component b) Type | % | Component c) Type | % | Component d) Type | % | Water % | Others Type | % |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Potato | 75.00 | hydrated vegetable fat | 1.25 | Lecithin | 1.5 | $TiO_2$ | 0.25 | 22.0 | - | - |
| 2 | Potato | 80.00 | hydrated vegetable fat | 1.0 | Lecithin | 0.9 | $TiO_2$ | 0.1 | 18.0 | - | - |
| 3 | Potato | 88.6 | hydrated vegetable fat | 0.8 | Lecithin | 0.5 | $SiO_2$ | 0.1 | 10.0 | - | - |
| 4 | Wheat | 78.0 | hydrated vegetable fat | - | Monoglycerid, $C_{18}$ | 5.0 | $SiO_2$ | 3.04 | 19.0 | dyestuff | 0.96 |
| 5 | Wheat | 79.0 | hydrated vegetable fat | 2.05 | - | - | $TiO_2$/ $SiO_2$ 1:1 | 0.95 | 18.0 | - | - |
| 6 | Wheat | 85.0 | hydrated animal fat | 4.80 | - | - | $TiO_2$ | 0.20 | 12.0 | - | - |
| 7 | Maize | 75.0 | hydrated animal fat | 4.80 | Monoglycerid, $C_{18}$ | 0.2 | $TiO_2$ | 0.15 | 17.0 | pre-cooked starch | 2.85 |
| 8 | Maize | 78.0 | hydrated animal fat | 3.0 | Monoglycerid $C_{18}$ | 1.0 | $TiO_2$ | 0.05 | 14.0 | pre-cooked starch | 3.95 |
| 9 | Rice | 79.0 | - | - | Monoglycerid $C_{18}$ | 2.0 | $SiO_2$ | 1.0 | 17.5 | dyestuff | 0.5 |
| 10 | Rice | 80.25 | hydrated animal fat | 0.9 | Diglyceride, $C_{18}$, $C_{16}$ | 0.6 | $SiO_2$ | 0.25 | 15.0 | Glycerin | 3 |
| 11 | Taploca | 75.2 | hydrated animal fat | 0.9 | Diglyceride, $C_{18}$, $C_{16}$ | 0.6 | $SiO_2$ | 0.3 | 21.0 | HMPCP | 2 |
| 12 | Potato | 73.96 | hydrated animal fat | 2.0 | Diglyceride, $C_{18}$, $C_{16}$ | 2.0 | $SiO_2$ | 0.04 | 17.0 | PEG 1000 | 5 |
| 13 | Potato | 75.25 | hydrated animal fat | 1.5 | Diglyceride, $C_{18}$, $C_{16}$ | 1.0 | $TiO_2$ | 0.25 | 18.0 | PEG 4000 | 4 |
| 14 | Potato | 75.25 | vegetable fat | 1.5 | Lecithin | 1.0 | $TiO_2$ | 0.25 | 18.0 | Sorbitol | 4 |
| 15 | Wheat | 60.00 | vegetable fat | 1.5 | Lecithin | 1.2 | $TiO_2$ | 0.25 | 17.0 | Polyacrylic acid | 20.05 |

## CLAIMS

1. A particulate, free-flowing starch based formulation comprising

(i) chemically unmodified starch or a mixture of chemically unmodified starch and no greater than 50%, by weight of the chemically unmodified starch, of another hydrophilic material, said starch or mixture being present in an amount of at least 72% by weight, based on the weight of the formulation;

(ii) a texturing agent in an amount of from 0.02% to 1.0% by weight, based on the weight of the formulation;

(iii) one, or a combination of both, of the following components: a lubricant/release agent and a melt-flow accelerator, the one component or the combination of both components being present in an amount of from 0.4% to 5.0% by weight, based on the weight of the formulation; and

(iv) water in an amount of at least 10%, based on the weight of the formulation.

2. A formulation according to Claim 1, wherein the chemically unmodified starch is a naturally occurring carbohydrate, obtained from one or more of the following sources: potatoes, rice, tapioca, corn, rye, oats, wheat or other plants, gelatinized starch, pre-cooked starch and highly water-soluble starch.

3. A formulation according to Claim 1 or 2, wherein the starch is potato starch or wheat starch.

4. A formulation according to Claim 1, 2 or 3 wherein the starch is present in an amount no greater than about 90% by weight, based on the weight of the formulation.

5. A formulation according to Claim 4, wherein the starch is present in an amount of from 75 to 85% by weight, based on the weight of the formulation.

6. A formulation according to Claim 5, wherein the starch is present in an amount of from 79 to 83% by weight, based on the weight of the formulation.

7. A formulation according to any preceding claim wherein the lubricant/release agent, when present, is present in an amount no greater than 3% by weight, based on the weight of the formulation.

8. A formulation according to any preceding claim, wherein the lubricant/release agent is present in an amount of from 0.6% to 1.2% by weight, based on the weight of the formulation.

9. A formulation according to any preceding claim, wherein the lubricant/release agent is an animal and/or vegetable fat.

10. A formulation according to Claim 9, wherein the lubricant/release agent is a hydrated animal or vegetable fat.

11. A formulation according to Claim 9 or 10, wherein the animal or vegetable fat is solid at room temperature.

12. A formulation according to Claim 9, 10 or 11, wherein the animal or vegetable fat has a melting point above 50°C.

13. A formulation according to any one of Claims 9 to 12, wherein the animal or vegetable fat is a triglyceride having a proportion of $C_{14}$-, $C_{16}$, $C_{18}$ fatty acids.

14. A formulation according to Claim 13, wherein the proportion of each fatty acid is as follows:
$C_{18}$ - approximately 65%;
$C_{16}$ - approximately 30%; and
$C_{14}$ - approximately 5%.

15. A formulation according to any preceding claim wherein the melt-flow accelerator is present in an amount of from 0.1 to 2% by weight, based on the weight of the formulation.

16. A formulation to any preceding claim, wherein the melt-flow accelerator is present in an amount of from 0.2 to 1% by weight, based on the weight of the formulation.

17. A formulation according to any preceding claim wherein the melt-flow accelerator is a solid mono- and/or diglyceride.

18. A formulation according to any preceding claim, wherein the melt flow-accelerator is a long chained fatty acid, for example a $C_{14}$-, $C_{16}$- or $C_{18}$- fatty acid or a phosphatide.

19. A formulation according to any preceding claim, wherein the melt-flow accelerator is lecithin.

20. A formulation according to any preceding claim, wherein the combined amount of the lubricant/release agent and the melt-flow accelerator is in the range of from 1 to 2.2% by weight, based on the weight of the formulation.

21. A formulation according to any preceding claim, wherein the texturing agent is titanium oxide and/or silicon dioxide.

22. A formulation according to Claim 21, wherein the titanium dioxide is present in an amount of about 0.25% and the silicon dioxide in an amount of about 0.1%, both percentages being by weight, based on the weight of the formulation.

23. A formulation according to any preceding claim, wherein the water is present in an amount no greater than 22% by weight based on the weight of the formulation.

24. A formulation according to any preceding claim, wherein the water is present in an amount of from 10 to 20% by weight, based on the weight of the formulation.

25. A formulation according to any preceding claim, wherein the water is present in an amount of from 15 to 19% by weight, based on the weight of the formulation.

26. A formulation according to any preceding claim, wherein component (i) of the formulation is the mixture of a chemically unmodified starch and another hydrophilic material in which the other hydrophilic material is present in an amount no greater than 20% by weight of the chemically unmodified starch.

27. A formulation according to Claim 26, wherein the other hydrophilic material is present in an amount of from 3 to 10% by weight of the chemically unmodified starch.

28. A formulation according to any preceding claim wherein the hydrophilic material is selected from:

gelatin, vegetable proteins such as: sunflower protein, soybean proteins, cotton seed proteins, peanut proteins, rape seed proteins, blood proteins, egg proteins, acrylated proteins; water-soluble polysaccharides such as: alginates, carrageenans, guar gum, agar-agar, gum arabic and related gums (gum ghatti, gum karaya, gum tragacanth), pectin; water-soluble derivatives of cellulose: alkylcelluloses hydroxyalkylcelluloses and hydroxyalkylalkycelluloses, such as: methylcellulose, hydroxymethycellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxyethylmethylcellulose, hydroxpropylmethylcellulose, hydroxybutylmethylcellulose, cellulose esters and hydroxyalkylcellulose esters such as: celluloseacetylphthalate (CAP), hydroxypropylmethylcellulosephthalate (HPCMP); carboxyalkylcelluloses, carboxyalkylalkylcelluloses, carboxyalkylcelluloseesters such as: carboxymethylcellulose and their alkli metal salts; water-soluble synthetic polymers such as: polyacrylic acids and polyacrylic acid esters, polymethacrylic acids and polymethacrylic acid esters, polyvinylacetates, polyvinylalcohols, poly vinylacetatephthalates (PVAP), polyvinylpyrrolidone, polycrotonic acids; suitable are also phthalated gelatin, gelatin succinate, crosslinked gelatin, shellac, water soluble chemical derivatives of starch, cationically modified acrylates and methacrylates possessing, for example, a tertiary or quaternary amino group, such as the diethylaminoethyl group, which may be quaternized if desired; and other similar polymers.

29. A formulation according to any preceding claim, further comprising a softening agent in an amount of from 0.5 to 10% by weight, based on the weight of the formulation.

30. A formulation according to Claim 29, wherein the softening agent is present in an amount of from 0.5 formulation.

31. A formulation according to Claim 29 to 30, wherein the softening agent is chosen from polyalkylene oxides, glycerin, glycerin mono-, di-, and triacetate; propylene glycol, sorbitol, sodium-diethylsulfosuccinate, triethylcitrate, tributylcitrate.

32. A formulation according to any preceding claim, wherein the total weight percentage of the water and softening agent does not exceed 22% by weight based on the weight of the formulation.

33. The use of a formulation according to any preceding claim in processing under applied pressure.

34. The use of a formulation according to any one of Claims 1 to 32 in pressure moulding, injection moulding, blow moulding or extrusion.

35. An article made under applied pressure from a formulation as claimed in any one of Claims 1 to 32.

36. An article according to Claim 35 being a pharmaceutical capsule.

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